PREVALENCE OF DRUG-RESISTANT STAPHYLOCOCCI IN TEHERAN UNIVERSITY HOSPITAL WARDS

F. Shafa, M.D., Ph. D.

Department of Microbiology, Faculty of Medicine, Teheran University, Iran.

Introduction

When Penicillin was first used in human therapy, about 12% of coagulase-positive strains of Staphylococcus were found to be relatively resistant to it (25,14,9). Nevertheless most of the clinicians believed that this problem would not constitute a major cause of therapeutic failure with penicillin (7,23). In practice however the wide-spread use of penicillin especially in hospital wards has been accompanied by the appearance of an increasing number of highly resistant strains of Staphylococcus (21,2,5,3,4,6,20,7,12).

The most extensive studies in this field have been carried out in London by Barber and his associates (2,3,5,4). In one of these studies Barber and Rozwadowska Dowzenko (5) have found that the number of resistant strains of Staphylococcus which was 14% in 1946, increased to 38% in 1947, and 59% in 1948. In places where penicillin is used intensively this number has now risen to 65-90%.

It has been stated in literature that penicillin resistant strains of Staphylococcus are most frequently encountered in hospital population where penicillin is used extensively (3,13,25,23), but it should be pointed out, firstly that penicillin is now being administered frequently outside hospitals, and secondly that penicillin resistant strains are spreading diffusely through the population by carriers who are found everywhere.

One of the most significant studies emphasizing the widespread distribution of these penicillin-resistant strains among healthy individuals is that of Martyn (19), in the obstetrical Department of St. Mary's Hospital, in Manchester, England. The nasopharynx and face of 130 healthy newborn infants were cultured for Staphylococci. None of the
babies or their mother had received penicillin. Staphylococci were obtained from the nasopharynx of 62% of infants, and from the faeces of 50%. Of the those strains isolated from the nasopharynx, 55.5% were penicillin-resistant, and 58.5% were resistant when cultured from the faeces.

Staphylococci have not only become resistant to penicillin, but also to the most current antibiotics.

At the section for sensitivity tests in the Department of Microbiology, Medical Faculty, Teheran University, it has been noticed that a great majority of Staphylococci were resistant to penicillin and a number of other antibiotics. It was decided therefore to ascertain the incidence of the drug-resistant strains of coagulase positive Staphylococcus by carrying out in vitro tests.

Materials and Methods

1) The strains of coagulase-positive Staphylococcus studied were isolated from the nose and wrist of nurses in Teheran University Hospital wards.
2) Coagulase test was performed in tubes with citrated rabbit plasma and 24 hours culture of staphylococcus. The mixtures were incubated at 37°C for 3 hours before reading the results.
3) Sensitivity tests were performed with high concentration of B.B.L.® Sensi-Discs.

Results

Table (1) shows the sensitivity of 50 coagulase-positive strains of Staphylococcus to penicillin, ten other antibiotics and the triple sulfa.

From this table the following results can be concluded:
1) At the present time only 18% of coagulase positive strains of Staphylococcus isolated from hospital nurses in Teheran University wards are susceptible to penicillin, the remainder are fully resistant (64%), moderately resistant (16%) or slightly resistant (12%).
2) With penicillin, aureomycin, tetracyclin, terramycin, chloramphenicol, Bacitracin and polymyxin-B, different ranges of susceptibility are observed, confirming the fact that in these antibiotics resistance develops slowly in a stepwise fashion.
3) In the case of streptomycin nearly one half of the strains (52%) are fully susceptible and the other half (48%) completely resistant

Table 1

<table>
<thead>
<tr>
<th>Antibiotics</th>
<th>Concentration</th>
</tr>
</thead>
<tbody>
<tr>
<td>Penicillin</td>
<td>10 units</td>
</tr>
<tr>
<td>Aureomycin</td>
<td>10 mg</td>
</tr>
<tr>
<td>Tetracyclin</td>
<td>15 mg</td>
</tr>
<tr>
<td>Terramycin</td>
<td>30 mg</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>50 mg</td>
</tr>
<tr>
<td>Bacitracin</td>
<td>20 mg</td>
</tr>
<tr>
<td>Polymyxin-B</td>
<td>5 mg</td>
</tr>
</tbody>
</table>

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showing that in this antibiotic, resistance develops suddenly.
4) Nearly all the strains under examination are still sensitive to newly
discovered antibiotics such as erythromycin, neomycin, and Kanamycin.
5) Strains which have become resistant to one member of tetracyclines
are resistant to other member (complete cross-resistance).
6) Strains which have become resistant to streptomycin are slightly
resistant to neomycin and Kanamycin (partial cross-resistance).

Discussion

1 - The origin and mechanism of drug-resistance:

a) All the available evidence indicates that the development of
drug-resistance both in vitro and in vivo is due to mutation. (22, 16, 1,
11, 2, 5, 15, 20).

These mutations occur spontaneously and independently of the
presence of drug. Their rate of occurrence is very low, being of the
order of $10^{-10}$ to $10^{-6}$. If the drug is present, the parent sensitive is
inhibited and the drug-resistant mutants can grow out. The action of
the drug is therefore not to stimulate the development of drug-resis-
tant forms but to select them.

b) Since nearly all penicillin-resistant strains of Staphylococcus
isolated from the body produce penicillinase, whereas resistant mutants
selected in the laboratory are not penicillinase producers, it can be con-
cluded that the production of penicillinase is not the only cause of
resistance, and other mechanisms such as alteration of bacterial meta-
bolism or permeability are also involved.

2 - Cross-resistance:

When microbial variants are resistant to a certain drug and are
selected out from the population by that drug, they may also be resis-
tant to another drug to which they have not been exposed. Such rela-
tionships exist principally between agents that are closely related
chemically, and may be the first clue to the identity of drugs whose
chemical structure has not been decided. Here is a list of some antibiot-
ica giving complete or partial cross-resistance.

a) Complete cross-resistance: Tetracyclin (Achromycin), chlorotetra-
cyclin (Aureomycin), and oxytetracyclin (Terramycin). Streptomy-
cin and dihydrostreptomycin. Kanamycin and Neomycin.

b) Partial cross-resistance: Streptomycin, neomycin, kanamycin
and clindamycin. Erythromycin and carbomycin.

3 - Hospital epidemiology:

Because of the increased prevalence of resistant strains of Sta-
phylococcus in hospitals, the danger of cross-infection and fatal compi-
cations in hospitalized patients has become a serious problem. For this
reason most of physicians and epidemiologists are trying to find practi-
cal solutions for prevention and control of staphylococcal infections in
hospitals. (10)

4 - Clinical implications:

From what has been said, it follows that in antibiotic therapy of Staphylococcal infections the following point should be taken into
consideration:

a) Before starting antibiotic therapy a sensitivity test should be performed, and among effective drugs the most current one should
be used.

b) The newly discovered antibiotics such as vancomycin and
Novobiocin should be used as little as possible, since with increase in
their use, an increase in the proportion of strains resistant to these
drugs must inevitably occur.

c) If the strain of staphylococcus is resistant to one antibiotic
the use of chemically related ones which give complete or partial cross-
resistance must be avoided.

d) The chemotherapeutic agents should not be casually admi-
istered as prophylactics or given for trivial infections from which the
patient would certainly recover.

Summary

1) Fifty coagulase positive strains of Staphylococcus isolated from the nose
and wrist of Hospital nurses have been examined for sensitivity to penicillin, teta-
cyclines, chloramphenicol, dihydrostreptomycin, erythromycin, neomycin, kanamycin,
bacitracin, polymyxin-B and the triple sulfa. The percentages of fully sensitive
strains at the present are as follows:

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>%</th>
</tr>
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<tbody>
<tr>
<td>Erythromycin</td>
<td>100%</td>
</tr>
<tr>
<td>Neomycin</td>
<td>78%</td>
</tr>
<tr>
<td>Kanamycin</td>
<td>78%</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>68%</td>
</tr>
<tr>
<td>Dihydrostreptomycin</td>
<td>55%</td>
</tr>
<tr>
<td>Penicillin</td>
<td>18%</td>
</tr>
</tbody>
</table>
### Prevalence of drug-resistant

<table>
<thead>
<tr>
<th>Drug</th>
<th>Percentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tetracyclines</td>
<td>16%</td>
</tr>
<tr>
<td>Polymyxin-B</td>
<td>1%</td>
</tr>
<tr>
<td>Triple sulfa</td>
<td>0%</td>
</tr>
</tbody>
</table>

2) The following topics have been discussed:
- a) The origin and mechanism of drug resistance
- b) Cross-resistance
- c) The hospital epidemiology of Staphylococcus
- d) The clinical implications of Staphylococcus drug-resistance.

### Résumé

1) Cinquante souches de staphylocoque à Coagulase positive ont été isolées de la cavité nasale et du poignet des infirmières de l'hôpital et leur sensibilité a été examinée à l'égard de Penicilline, de Tetracycline, de chloramphénicol, de Dihydrostreptomycine, d'Erythromycine, de Neomycine, de Kanamycine, de Bacitracine, de Polymyxin-B et de Triple-sulfa. Le pourcentage de souches pleinement sensibles est actuellement comme suit:

<table>
<thead>
<tr>
<th>Antibiotique</th>
<th>Pourcentage</th>
</tr>
</thead>
<tbody>
<tr>
<td>Erythromycine</td>
<td>100%</td>
</tr>
<tr>
<td>Neomycine</td>
<td>75%</td>
</tr>
<tr>
<td>Kanamycine</td>
<td>75%</td>
</tr>
<tr>
<td>Chloramphenicol</td>
<td>60%</td>
</tr>
<tr>
<td>Dihydrostreptomycine</td>
<td>50%</td>
</tr>
<tr>
<td>Penicilline</td>
<td>10%</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>10%</td>
</tr>
<tr>
<td>Polymyxin-B</td>
<td>1%</td>
</tr>
<tr>
<td>Triple-Sulfa</td>
<td>0%</td>
</tr>
</tbody>
</table>

Les problèmes suivants ont été discuté:
- a) L'origine et mécanisme de résistance médicamenteuse.
- b) La résistance croisée.
- c) L'épidémiologie de staphylocoque de l'hôpital.
- d) Les implications cliniques des staphylococques résistants.

### References


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